# Chapter 5: Referral to specialists and models of care

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Early identification and referral of people with CKD has the potential to reverse, delay, or prevent progression of disease and is a key focus of international initiatives in the area of kidney disease. The goals of early identification and referral are several-fold and include:

1. Provision of specific therapy based on diagnosis
2. Slowing/arresting CKD progression
3. Evaluation and management of comorbid conditions
4. Prevention and management of CVD
5. Identification, prevention, and management of CKD-specific complications (e.g., malnutrition, anemia, bone disease, acidosis)
6. Planning and preparation for RRT (e.g., choice of modality, access-placement and care, preemptive transplantation)
7. Psychosocial support and provision of conservative care and palliative care options where required

## 5.1: REFERRAL TO SPECIALIST SERVICES

**5.1.1: We recommend referral to specialist kidney care services for people with CKD in the following circumstances (*1B*):**

- **AKI or abrupt sustained fall in GFR;**
- **GFR $<30$ ml/min/1.73 m$^2$ (GFR categories G4-G5)*;**
- **a consistent finding of significant albuminuria (ACR $\geq 300$ mg/g [$\geq 30$ mg/mmol] or AER $\geq 300$ mg/24 hours, approximately equivalent to PCR $\geq 500$ mg/g [$\geq 50$ mg/mmol] or PER $\geq 500$ mg/24 hours);**
- **progression of CKD (see Recommendation 2.1.3 for definition);**
- **urinary red cell casts, RBC $>20$ per high power field sustained and not readily explained;**
- **CKD and hypertension refractory to treatment with 4 or more antihypertensive agents;**
- **persistent abnormalities of serum potassium;**
- **recurrent or extensive nephrolithiasis;**
- **hereditary kidney disease.**

**5.1.2: We recommend timely referral for planning renal replacement therapy (RRT) in people with progressive CKD in whom the risk of kidney failure within 1 year is 10-20% or higher†, as determined by validated risk prediction tools. *(1B)***

### RATIONALE

This statement reminds the practitioner that there is a need for timely referral for RRT planning in order to ensure good decision making and outcomes. The use of the word 'timely' is vague as this is not yet determined, and is based on patient and system factors. The actual amount of time required at a minimum is at least 1 year to ensure appropriate education, understanding and referrals to other practitioners (e.g., vascular access surgeons, transplant teams, etc). The second part of the statement refers to the fact that those who are progressing (versus those who are stable) are the ones who will benefit from this referral. Hence, there is a need to apply prediction tools to help identify the risk of progression. We have not stated which prediction tool is preferred as these may differ depending on information available in any individual or local experience. Examples of prediction tools can be found in recent publications.[257,260,261]

The scope of nephrology practice includes a wide variety of conditions including not only ESRD but also acute and chronic primary and systemic diseases involving individual elements of the kidney, resistant hypertension, and biochemical derangements. There are thus more potential benefits of nephrology referral than those widely recognized such as identification of reversible causes of CKD, provision of treatment that may slow progression of CKD, management of the metabolic complications of advanced CKD, and preparation for dialysis and transplantation.

In certain people, such as those with diabetes, transition to a severe reduction in GFR and kidney failure may progress rapidly. In such individuals early nephrology referral is the watchword but when an individual's kidney function is relatively stable (rate of decline in GFR $<5$ ml/min/1.73 m$^2$/year), we suggest using the grid as a guide (Figure 21). Where refer is marked by an asterisk, referring clinicians may wish to discuss with their nephrology service depending on local arrangements.

### Evidence Base

Although referral recommendations in the literature are inconsistent, criteria for nephrology referral include SCr or GFR, proteinuria, hematuria, BP, and electrolyte derange-

*If this is a stable isolated finding, formal referral (i.e., formal consultation and ongoing care management) may not be necessary and advice from specialist services may be all that is required to facilitate best care for the patients. This will be health-care system dependent.

†The aim is to avoid late referral, defined here as referral to specialist services less than 1 year before start of RRT.

| GFR categories (ml/min/ 1.73 m²) Description and range | | | | Persistent albuminuria categories Description and range | | |
|---|---|---|---|---|---|---|
| | | | | A1 | A2 | A3 |
| | | | | Normal to mildly increased | Moderately increased | Severely increased |
| | | | | <30 mg/g <3 mg/mmol | 30–300 mg/g 3–30 mg/mmol | >300 mg/g >30 mg/mmol |
| | G1 | Normal or high | ≥90 | | Monitor | Refer* |
| | G2 | Mildly decreased | 60–89 | | Monitor | Refer* |
| | G3a | Mildly to moderately decreased | 45–59 | Monitor | Monitor | Refer |
| | G3b | Moderately to severely decreased | 30–44 | Monitor | Monitor | Refer |
| | G4 | Severely decreased | 15–29 | Refer* | Refer* | Refer |
| | G5 | Kidney failure | <15 | Refer | Refer | Refer |

**Figure 21 | Referral decision making by GFR and albuminuria.** *Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referring. GFR, glomerular filtration rate. Modified with permission from Macmillan Publishers Ltd: *Kidney International*. Levey AS, de Jong PE, Coresh J, *et al.*[30] The definition, classification, and prognosis of chronic kidney disease: a KDIGO controversies conference report. Kidney Int 2011; 80: 17-28; accessed http://www.nature.com/ki/journal/v80/n1/full/ki2010483a.html

ment.[670] Data relating to referral for those with glomerular disease, hypertension, AKI, and diabetes may be found in the relevant guidelines.[7,8,10,262]

In this section we will briefly consider summaries of the evidence relating to timely referral for planning RRT in people with progressive CKD. In this aspect the literature concerning late referral in the last quarter of a century has been remarkably consistent; both studies and narrative reviews identifying a number of adverse consequences of late referral and related benefits of early referral (Table 35).

Patients who are aged >75 years, female, non-Caucasian, uninsured, of lower socioeconomic or educational status, or have multiple comorbidities are most at risk for non-referral for CKD care.[671,672] Patients with kidney disease have never been randomized to early or late referral to nephrology services and the definition of late referral in the published studies varies; three months is probably less than the absolute minimum amount of time required for assessment, education, preparation for RRT and creation of access but is the most frequently employed definition. Overall there are more than 50 studies in the published literature and a meta-analysis of 22 of these studies from 10 different countries serves to underline some of the key messages (Table 36), giving an indication of the size of the differences in mortality and hospital length of stay and also highlighting the significantly lower serum albumin level in late referred patients.[673]

A systematic review considered twenty-seven longitudinal cohort studies providing data on 17,646 participants of whom 11,734 were referred early and 5912 (33%) were referred late.[674] OR for mortality reductions in patients referred early were evident at 3 months (OR 0.51; 95% CI 0.44-0.59; $P<0.0001$) and remained significant at 5 years (OR 0.45; 95% CI 0.38-0.53; $P<0.0001$). Initial hospitalization was 8.8 days shorter with early referral (95% CI -10.7 to -7.0 days; $P<0.0001$). Differences in mortality and hospitalization data between the 2 groups were not explained by differences in prevalence of diabetes mellitus, previous CAD, BP control, serum phosphate, and serum albumin. Early referral was associated with better preparation and earlier placement of dialysis access and better uptake of peritoneal dialysis.

Over a decade ago McLaughlin et al. evaluated the cost implications of early versus late referral.[675] Outcomes of interest were total cost of patient care, patient life-years, patient life-years free of RRT and hospital length of stay. Mean total costs per patient over five years were US$87,711 and US$110,056 for early and late referrals, respectively. The mean patient life-years were 3.53 and 3.36 years, respectively, and the patient life-years free of RRT were 2.18 and 1.76 years, respectively. Those patients referred early spent significantly less time in hospital (length of stay 25 days versus 41 days). Klebe et al. subsequently investigated the annualized cost of implementation of referral guidelines for CKD.[676] Although CKD guideline implementation resulted in significant increases in nephrology referral and additional investigation, they estimated that the associated costs could

**Table 35 | Early versus late referral: consequences and benefits**

| Consequences of late referral | Benefits of early referral |
|---|---|
| Anemia and bone disease | Delay need to initiate RRT |
| Severe hypertension and fluid overload | Increased proportion with permanent access |
| Low prevalence of permanent access | Greater choice of treatment options |
| Delayed referral for transplant | Reduced need for urgent dialysis |
| Higher initial hospitalization rate | Reduced hospital length of stay and costs |
| Higher 1-year mortality rate | Improved nutritional status |
| Less patient choice of RRT modality | Better management of CVD and comorbid conditions |
| Worse psychosocial adjustment | Improved patient survival |

Abbreviations: CVD, cardiovascular disease; RRT, renal replacement therapy.

**Table 36 | Outcomes of early versus late referral**

| Variable | Early referral mean (SD) | Late referral mean (SD) | P value |
|---|---|---|---|
| Overall mortality, % | 11 (3) | 23 (4) | $<0.0001$ |
| 1-year mortality, % | 13 (4) | 29 (5) | 0.028 |
| Hospital length of stay, days | 13.5 (2.2) | 25.3 (3.8) | 0.0007 |
| Serum albumin at RRT start, g/dl [g/l] | 3.62 (0.05) [36.2 (0.5)] | 3.40 (0.03) [34.0 (0.3)] | 0.001 |
| Hematocrit at RRT start, % | 30.54 (0.18) | 29.71 (0.10) | 0.013 |

Abbreviation: RRT, renal replacement therapy.
Adapted from Am J Med, Chan MR, Dall AT, Fletcher KE, *et al.*[673] Outcomes in patients with chronic kidney disease referred late to nephrologists: a meta-analysis. 120: 1063-1070, 2007, with permission from Elsevier; accessed http://download.journals.elsevierhealth.com/pdfs/journals/0002-9343/PIIS000293430700664X.pdf

be recouped by delaying dialysis requirement by 1 year in one individual per 10,000 patients managed according to guidelines.

### International Relevance

Local practice and resource will dictate local referral practice but regardless of the health-care system, delay or prevention of progression of both CKD and complications associated with CKD will add value. Local organizations will determine the best methods of communication and interaction between patients, specialists, and primary care physicians.

### Implications for Clinical Practice and Public Policy

Implementation of referral guidelines will inevitably lead to an increased workload for specialist nephrology services. However, introduction of local initiatives in conjunction with primary care providers can improve the appropriateness and quality of the referral. Local initiatives combined with national policy and practice changes can lead to an improvement in the outcomes of CKD patients regardless of the level of resource available.

### Pediatric Considerations

Current pediatric practice in most areas of the world would suggest a higher level of kidney function for referral than that for adults, though the principles remain the same. Much of the pediatric nephrologist's consultation occurs from infants, or even antenatal sources, where the identification of the child as being 'at-risk' may be apparent from radiographic studies performed *in utero*. The relatively non-specific signs and symptoms of most forms of renal disease in the young child mandates a higher level of suspicion in the referring physician, and a lower threshold of acceptance of the consult in the subspecialty clinic accepting these referrals.

Attempts to develop universal guidelines for referral of children to pediatric nephrology services would be dependent on local resources (as is the case for adults) and it is of value to consider in broad categories the types of conditions for which referral to a pediatric nephrologist would be expected to provide benefit to the referring physician and patient/family.

In a recent review Barakat[677] attempts to address a number of these issues by outlining the most common presentations of a child with significant renal disorders. Barakat and Chesney also suggest a number of specific areas in terms of initial investigations, management, and follow-up where the primary care physician can legitimately play a role in the care of the child with renal disease and provides a list of suggested referral triggers.[678]

While there will be variation in referral triggers, referral would be recommended for the following: acute or chronic reduction in renal function, poorly treated or severe hypertension, severe electrolyte abnormalities, the finding of significant abnormalities in urinary tract structure, or the presence of systemic diseases likely to produce renal effects. Similarly, the need for education in progressive conditions, performance of and interpretation of renal biopsies, and allaying parental/patient anxiety would also be acceptable reasons for referral.

There is no 'minimum acceptable value' of renal dysfunction below which one can be certain to see significant abnormalities in clearance, electrolyte, or other side effects associated with progressive renal disease in children such as growth failure or neurocognitive issues. However, the

KDOQI CKD Guidelines[1] stated that while a child with a eGFR $<30$ ml/min/1.73 $m^2$ warranted referral to a pediatric nephrologist in all cases, that in fact it was also reasonable to consider any child with evidence of CKD– and in particular those with eGFR $<60$ ml/min/1.73 $m^2$ – for referral to a pediatric nephrologist regarding evaluation and management.[43]

It is reasonable to presume that, as in adults, the concept of referral 'early' or 'above' some minimum level of function should allow for numerous benefits to the patient and family, but again there are few data for this in children. The most informative information on both of these issues can be derived from two papers examining the issue of late referrals of children who eventually required ESRD care. Kennedy et al.[679] demonstrated that at the time of referral to their center, the children $>1$ year of age had a median Schwartz eGFR of only 27 (IQR 9-52) ml/min/1.73 $m^2$, and in fact 55% of these children over the age of 1 year were referred with an eGFR $<30$ ml/min/1.73 $m^2$, meeting one of two definitions of a late referral. When they considered their second definition of initiation of RRT within 90 days of referral, commonly used in the literature for this particular topic, 30% of the eligible cohort required RRT within that 90-day window and hence were considered late referrals on this basis. The potential effect on the child's health could be ascribed to such a delay in referral: those children had lower mean Hb (8.7 $\pm$ 0.6 g/dl [87 $\pm$ 6 g/l]) versus (12.8 $\pm$ 0.6 g/dl [128 $\pm$ 6 g/l]) and higher median urea (34 (IQR 5-14) mmol/l [203 (IQR 30-84) mg/dl] versus 6 (IQR 5-14) mmol/l [36 (IQR 30-84) mg/dl], $P<0.001$) than those who presented with eGFR $>30$ ml/min/1.73 $m^2$. Secondary analysis confirmed this was also true in the groups if one looked at those above or below an eGFR of 60 ml/min/1.73 $m^2$. The second paper by Boehm and colleagues[680] was a retrospective single pediatric center report that demonstrated that over $\sim$30 years of referrals (N = 111), 24% of them could be considered as late referrals, as defined by need for RRT within 90 days of referral. In this late referral group, the eGFR (Schwartz) was significantly lower than those presenting later, (14.9 versus 34.2 ml/min/1.73 $m^2$, $P<0.001$) as was the Hb at presentation (8.0 g/dl [80 g/l] versus 10.5 $\pm$ 2.3 g/dl [105 $\pm$ 23 g/l]; $P<0.001$). Importantly the Hb deficit persisted at the time of RRT initiation, with the Hb in the late referral group being 8.5 g/dl [85 g/l] versus 9.8 $\pm$ 1.9 g/dl [98 $\pm$ 19 g/l] in the earlier referred patients, $P<0.01$. The other metric of interest chosen by these authors to evaluate the possible detrimental effect of late referral was the likelihood of a given child having a pre-emptive transplant, i.e., prior to dialysis initiation. While this association was not confirmed in Kennedy's paper, Boehm and his group demonstrated that in their patient population children who were referred late only 11% were preemptively transplanted as compared to 40% of children who presented to care more than 90 days prior to the need for some form of RRT. Of further interest, although somewhat counterintuitive, the proportion of patients in the Boehm study who initiated hemodialysis was not statistically different between those in the late versus early referral groups, 62% versus 67%, $P<0.05$ respectively.

The underlying concept of referral to a pediatric nephrologist in the face of rapid progression of renal failure is of course applicable in full. However, no current validated risk of progression tool exists in pediatric nephrology. As to what level of functional decline might be considered 'concerning,' the best evidence is derived from the longitudinal iohexol GFR data as accrued in the CKiD trial. Data from that study related to the annualized rate of decline in renal function for children with glomerular conditions is $-10.5\%$ as compared to those with a non-glomerular causes in whom the annualized rate of change is only $-3.9\%$.[71] Any child whose rate of decline exceeded these two values would at least warrant much closer follow-up and/or investigation for modifiable factors to slow progression. Note this is not to say these rates of decline should be considered to be 'normal' for either category. All efforts to slow decline in renal function would still be of vital importance in every individual.

## 5.2: CARE OF THE PATIENT WITH PROGRESSIVE CKD

The following section describes recommended structures and key milestones for people with progressive CKD. The recommendations are intended to model best practices but it is appreciated that different health-care systems, geographical issues, and economic considerations will have variable abilities to implement these recommendations.

Key aspects of caring for people with progressive CKD, as they approach end of life or RRT options are addressed in this section.

**5.2.1: We suggest that people with progressive CKD should be managed in a multidisciplinary care setting. (*2B*)**

**5.2.2: The multidisciplinary team should include or have access to dietary counseling, education and counseling about different RRT modalities, transplant options, vascular access surgery, and ethical, psychological, and social care. (*Not Graded*)**

### RATIONALE

Optimal care is that care which leads to the best outcomes for the individual, the population, and society. The model of care varies according to CKD severity, which will determine the target population and goals. These statements are worded to predominantly encompass those people likely to progress to ESRD. CKD models of care follow the same principles embodied in the chronic disease model of care (Figure 22). The specific components for CKD models of care include: protocols for laboratory and clinic visits; attention to cardiovascular comorbidities and CKD-associated comorbidities such as anemia; a vaccination program (see Recommendation 4.6.1-4.6.6); an education program which includes both general CKD and RRT education (including conservative management where appropriate); self-management; lifestyle modification including diet, exercise, and smoking

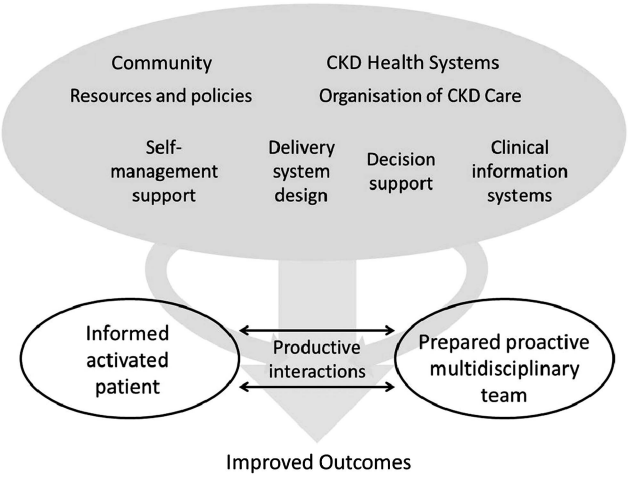


**Figure 22 | The CKD chronic care model**. CKD, chronic kidney disease. Adapted by permission from BMJ Publishing Group Limited. Improving the quality of health-care for chronic conditions. Epping-Jordan JE, Pruitt SD, Bengoa R, *et al.*[681] Qual Saf Health Care. 13: 299-305, 2004; accessed http://qualitysafety.bmj.com/content/13/4/299.full.pdf+html

cessation; and counseling and support for factors such as social bereavement, depression, and anxiety.

#### International Relevance

Standardized and culturally appropriate protocols should be considered. While it is recognized that resources may vary across and within jurisdictions, recommendations here are based on principles of care, which should be relevant across the globe.

#### Implications for Clinical Practice and Public Policy

CKD is a complex condition and co-exists with many other conditions. Therefore models of care should be developed that integrate the complexity of the clinical conditions involved, patient-centered philosophies, and the health-care environment. The principles of care are universal but implementation may be customized to specific circumstances.

#### Pediatric Considerations

Papers addressing the need for and effectiveness in the utility of multidisciplinary clinics for management of pediatric CKD patients have been published. In 2012, Ajarmeh et al.[682] described a retrospective comparison of two cohorts of children aged 0-18 years of age and followed at a single Canadian tertiary care referral center over a 1-year time period either before or following the full implementation of a multidisciplinary CKD clinic which included the services of dedicated pediatric nephrologists, renal nursing, pharmacy, dietitians, social workers, and a renal database manager. In 2009, Menon et al.[683] published data from a large American pediatric referral center and compared the outcomes of children from one of two 5-year cohorts in the period immediately preceding or following the initiation of a specific Chronic Renal Insufficiency clinic which was staffed by pediatric nephrologists, nurse clinicians, transplant coordinators, dietitians, social workers, and a psychologist.

Ajarmeh et al.[682] compared the two cohorts in a number of areas during their year of follow-up whereas Menon et al.[683] chose to look at each individual patient in the 12 months immediately prior to initiating RRT. While the studies had different variables of interest and used slightly different approaches for comparison of results between their groups, both demonstrated a reduction in the rate of decline in estimated renal function, improved Hb levels, and improvement in at least some aspect of bone mineral metabolism control in their respective cohorts cared for in the multidisciplinary era. In addition, both studies also demonstrated a decrease in resource utilization by patients in the multidisciplinary clinic as measured by median length of stay[682] and number of unplanned admissions per patient per year.[683] Also of note, Menon *et al*. demonstrated that in the patients who initiated dialysis (which was how the cohort was chosen), more patients who started hemodialysis did so with a functioning arteriovenous fistula or arteriovenous graft at the time of initiation compared to those from the general nephrology clinic era (85.7 versus 20%, $P = 0.02$).

### 5.3: TIMING THE INITIATION OF RRT

**5.3.1: We suggest that dialysis be initiated when one or more of the following are present: symptoms or signs attributable to kidney failure (serositis, acid-base or electrolyte abnormalities, pruritus); inability to control volume status or blood pressure; a progressive deterioration in nutritional status refractory to dietary intervention; or cognitive impairment. This often but not invariably occurs in the GFR range between 5 and 10 ml/min/1.73 $m^2$. (*2B*)**

**5.3.2: Living donor preemptive renal transplantation in adults should be considered when the GFR is $<20$ ml/min/1.73 $m^2$, and there is evidence of progressive and irreversible CKD over the preceding 6-12 months. (*Not Graded*)**

#### RATIONALE

The statement is worded very precisely to highlight the need for RRT to address symptoms and to avoid the institution of dialysis therapy at an arbitrary number representing the degree of residual renal function. Given the risks and benefits of RRT, as well as the potential imprecision of measurements, patients need to be treated according to symptoms and signs, not simply based on a laboratory value.

Data from national registries has shown a consistent rise in GFR at initiation of RRT. This rise has been driven partly by a desire to improve nutritional status and also by earlier observational data suggesting adverse outcomes associated with RRT initiation at lower GFR. These early data were subject to much confounding. RCT data, supported by large registry-based studies corrected for confounding, show no survival advantage to early start dialysis (Initiating Dialysis

Early and Late [IDEAL] study, see Evidence Base Below). Thus, the statement as written should help the clinician to balance symptoms with laboratory values in decision making.

The statement regarding living donor transplantation is intended to ensure that practitioners think about this option in the context of the totality of RRT options. It is worded to be concordant with local living donation transplant policies. It aims to reflect the need for risk-benefit assessment of preemptive renal transplantation in all individuals. Note that the statement asks clinicians to consider this option, but does not state at which level of GFR the preemptive transplant would occur as this is a matter of local practice and patient-specific considerations.

#### Evidence Base

The perceived survival advantage of early start of dialysis was questioned by a study from the Netherlands Cooperative Study on the Adequacy of Dialysis Study Group (NECOSAD).[684] Of 253 patients with new ESRD, 94 (37%) started dialysis late (GFR 4.9 ± 1.7 ml/min/1.73 $m^2$) and 157 started in a timely fashion (GFR 7.1 ± 2.4 ml/min/1.73 $m^2$). Although there was a small gain in survival time over 3 years after start of dialysis for the timely start group (2.5 months) there was no significant difference in survival between the 2 groups and the gain in survival time was offset by an estimated lead-time bias of between 4.1 and 8.3 months. In a study eliminating the effect of lead-time bias Traynor et al. found no benefit in survival in those initiating dialysis early.[685] Subjects starting dialysis early (N = 119) had a median IQR CrCl of 10.4 (9.1-11.9) ml/min versus 6.7 (5.6-7.5) ml/min in 116 subjects starting dialysis late. After correction for multiple confounders, they found an 11% greater hazard for mortality with each 1 ml/min increase in CrCl at start of dialysis (HR 1.11; 95% CI 1.01-1.21; P = 0.024). Subsequent observational studies, including large dialysis registry studies from around the globe, have all suggested increased mortality when dialysis is started early.[686–696] These studies encountered multiple difficulties in drawing conclusions from this observational approach including lead-time bias, problems with estimating GFR from SCr in people with low muscle mass and/or fluid overload, the fact that people with symptoms and/or increased comorbidity are more likely to start dialysis early, and finally survivor bias in studies including people only when they start dialysis (and therefore excluding those who die prior to starting diaysis). These confounders were largely addressed by a multicenter controlled trial in which 828 adults with progressive CKD and CrCl 10-15 ml/min/1.73 $m^2$ were randomly assigned to early (CrCl 10-14 ml/min [0.17-0.23 ml/s]) or late (CrCl 5-7 ml/min [0.08-0.12 ml/s]) initiation of dialysis.[697] The study protocol allowed an earlier start where deemed clinically necessary by investigators and although the difference in GFR at dialysis initiation between the 2 groups was significant (early start CrCl 12.0 versus late start 9.8 ml/min, MDRD GFR 9.0 versus 7.2 ml/min/1.73 $m^2$), it was less than planned because 19% of early starters started late and 76% of late starters started early. There was no difference in mortality between the early and late start groups and no difference in the study's secondary outcomes (cardiovascular events, infectious events and complications of dialysis) between the 2 groups. Finally, a further observational study sought to examine the effect of early initiation of dialysis on survival in a 'healthy' group of 81,176 subjects with ESRD aged 20-64 years, without diabetes, and with no comorbidity other than hypertension.[698] The unadjusted 1-year mortality by MDRD GFR at dialysis initiation ranged from 6.8% in the reference group (GFR < 5.0 ml/min/1.73 $m^2$) to 20.1% in the highest GFR group (≥ 15.0 ml/min/1.73 $m^2$). In an even healthier subset of 35,665 subjects with serum albumin concentrations of 3.5 g/dl or higher prior to hemodialysis initiation, the 1-year mortality was 4.7%. In this group the adjusted HR for mortality was 1.27 for GFR 5.0-9.9 ml/min/1.73 $m^2$, 1.53 for GFR 10.0-14.9 ml/min/1.73 $m^2$, and 2.18 for GFR ≥ 15.0 ml/min/1.73 $m^2$ compared with the reference group of GFR < 5.0 ml/min/1.73 $m^2$.

#### International Relevance

The availability of resources for formal multidisciplinary teams, educational materials, and access to specialized counseling for diet, advance directives, access planning, and pre-emptive transplantation varies around the world. These statements are proposed so that 'best practices' can be documented or aspired to. The need for education, planning, and appropriate expertise for the management of this patient group is internationally relevant. The methods, frequency, and tools with which this can be accomplished will be region specific.

#### Implications for Clinical Practice and Public Policy

There is a need to focus on regular symptom assessment as part of CKD review in those with lower eGFR values. Individual assessment and availability of resources will dictate specific timing of therapies.

Clinicians should be aware of the impact of early dialysis start on QOL[699] before recommending this strategy to patients.

#### Pediatric Consideration

***Timing of initiation of dialysis.*** As might be expected, information as to the proper timing for initiation of dialysis does not exist for children. Thus, it would seem reasonable to follow the guidelines as set out for the adults. A review by Greenbaum and Schaefer[700] provides the reader with generally agreed upon absolute and relative indications for initiation of dialysis in the child. The absolute indications listed are those of neurologic consequences attributable to uremia; hypertension that fails to respond to antihypertensive therapy; pulmonary edema unresponsive to diuretics; pericarditis; bleeding tendency; and refractory nausea or vomiting. However, the authors clearly state that there is no current consensus as to the validity of the relative indications and specifically the level at which each engenders the need for

dialysis. Relative indications to commence dialysis include less severe uremic symptoms, hyperkalemia, hyperphosphatemia, malnutrition, and growth failure. The authors point out as well that the answer to 'early' versus 'late' dialysis initiation cannot be addressed in any meaningful way in children as there is currently lack of data; and the unique factors to consider in a child such as growth, psychosocial development, likely renal transplant, and need for extended time on both dialysis and in transplant make the probability of a clinical trial to address this issue nearly impossible.

*Timing of living donor transplant.* There is no direct evidence to guide the pediatric nephrologist as to the 'best' timing for a living donor transplant in children. In each individual case the relative likelihood of improvement in presumed uremic symptoms and burden of disease as related to management of CKD will need to be balanced against the risks of transplant surgery itself and the attendant medication risks with prolonged immunosuppression. While there is little doubt as to the benefit in overall lifespan accrued by a child who is transplanted as opposed to one maintained on standard dialysis therapies during their childhood (average life expectancy of 63 versus 38 years respectively),[701] the issue as to what level of residual function is sufficient to justify delay or conversely proceeding to transplant is simply not readily available.

It should also be noted that reliance on GFR as the sole marker of disease intensity is unlikely to be sufficient for making such a decision, and patient symptoms and/or unique family factors may play a significant role in the decision as to timing of a living donor transplant (e.g., a young grandparent available and healthy to donate at age 60 years may not be eligible at age 63 years and so an earlier transplant would be favored).

## 5.4: STRUCTURE AND PROCESS OF COMPREHENSIVE CONSERVATIVE MANAGEMENT

**5.4.1: Conservative management should be an option in people who choose not to pursue RRT and this should be supported by a comprehensive management program. (*Not Graded*)**

**5.4.2: All CKD programs and care providers should be able to deliver advance care planning for people with a recognized need for end-of-life care, including those people undergoing conservative kidney care. (*Not Graded*)**

**5.4.3: Coordinated end-of-life care should be available to people and families through either primary care or specialist care as local circumstances dictate. (*Not Graded*)**

**5.4.4: The comprehensive conservative management program should include protocols for symptom and pain management, psychological care, spiritual care, and culturally sensitive care for the dying patient and their family (whether at home, in a hospice or a hospital setting), followed by the provision of culturally appropriate bereavement support. (*Not Graded*)**

### RATIONALE

These statements are intended to highlight the need for comprehensive conservative care processes and resources in the care of this complex patient group. There is increasing recognition that provision of organized care to those who are dying or choose to not pursue dialysis and transplant care is of value to the patients and their families. Clinicians involved in caring for these patients should be alerted to this need. These statements are positioned so as to overtly state this need.

In different societies or cultural areas, the form and structure of this care may vary tremendously and families or religious organizations may be able to deliver expert and sensitive care. The details here are listed not to be prescriptive but rather to articulate the 'best practices' in communities where resources may be available and to serve a construct to review in those locations where resources are more limited.

### Evidence Base

The evidence base for these statements is limited to documents describing the burden of illness and unmet needs in patients with CKD as they decide either not to pursue dialysis or to withdraw from RRT. As the readers will appreciate, there are neither RCTs nor even large cohort studies to inform these statements within the CKD populations. Analogies with oncology have been drawn and literature from there has been used to justify the concepts above.

Patients with advanced CKD have extensive palliative care needs for years before death. Throughout their illness trajectory, symptom burden is high.[702–707] The number and severity of physical and emotional symptoms are similar to those of cancer patients hospitalized in palliative care settings.[703,708] Advanced CKD patients managed without dialysis are equally symptomatic.[706] An increasing number of dialysis patients die after withdrawal of dialysis (10-15% in 1990, 20% in 2004), primarily due to poor QOL, representing the second leading cause of death after CVD.

Conservative care focuses on slowing the decline in renal function, actively managing symptoms, advance care planning, and the provision of appropriate palliative care. In oncology, receiving early palliative care is associated with better QOL, fewer emergency department visits and hospitalizations, less aggressive care at the end of life, and surprisingly, longer survival.[709] These observations suggest that development of clinical models that integrate appropriate palliative care, including the creation of conservative care pathways, are likely to be hugely beneficial and would help avoid harmful dialysis to those patients unlikely to realize benefit. Such conservative care programs are slowly being developed, primarily in the UK and Canada.

The literature describing experiences of specific programs and symptom burden in CKD, as well as advocating for better care, has only become more prevalent since 2005.[709–716]

Poor quality, hospitalized deaths began to improve for patients dying with cancer as a result of an increasing emphasis on palliative care teams providing attention to symptom control, psychosocial needs, and options for location of care. The literature suggests that current models of palliative care for cancer patients that deinstitutionalized health-care services have not only improved patient outcomes and quality of care[717–720] but have been cost-neutral.[721]

#### International Relevance

All countries have people with CKD who withdraw either voluntarily or involuntarily from dialysis services. Best care for those patients will obviously need to respect cultural and religious values, but would necessarily be based on the same philosophical grounds of maintaining dignity of the individual. Appreciating the need for and articulating conservative care pathways overtly would be internationally applicable.

#### Implications for Clinical Practice and Public Policy

There is a need to ensure appropriate access to services and education surrounding quality care during terminal stages of a chronic condition. There is increasing attention to this in many societies but not in all. Appreciating the variability in the resources required and their availability to different groups of patients is important for implementation. Furthermore, involvement of religious and cultural leaders in recognition of these care practices can be enhanced if they are overtly recognized as part of the care continuum.

There is a need for robust assessment of best practices in CKD and other chronic conditions so that we may provide best care throughout the continuum of life. Researchers around the world are actively pursuing this so that we may have better tools, programs, and ultimately, better outcomes for our patients.

#### Pediatric Consideration

Despite the lack of published evidence, there is no reason to believe that children and families faced with the need to consider conservative care or a palliative approach to their impending ESRD would not benefit from all of the above recommendations. It would seem reasonable for pediatric nephrology centers to liaise with their pediatric oncology or palliative care teams, ethicists, and pastoral care providers to assist them in developing, defining, and/or identifying locally available resources for situations where a child is not deemed a candidate for RRT prior to their occurrence.